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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,098	11/21/2006	Jeffrey W. Strovel	689290-253	9106

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EXAMINER	
SHAW, AMANDA MARIE	
ART UNIT	PAPER NUMBER
1634	
MAIL DATE	DELIVERY MODE
03/31/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,098	STROVEL ET AL.	
	Examiner	Art Unit	
	Amanda Shaw	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-25,28-30,32-34,36,56-58,62,67-72,75,76 and 79-83* is/are pending in the application.

4a) Of the above claim(s) *9-25,28-30,32-34,36,56-58,62,67-72,75,76 and 79-83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/11/2010, 2/19/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the amendment filed February 16, 2010. This action is made FINAL.

Claims 5-25, 28-30, 32-34, 36, 56-58, 62, 67-72, 75-76, and 79-83 are currently pending.

Claims 5 and 8 have been amended.

Claims 9-25, 28-30, 32-34, 36, 56-58, 62, 67-72, 75-76, and 79-83 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on August 24, 2009.

Withdrawn Objections

2. The objections made to claims 5 and 8 in section 2 of the Office Action of November 9, 2009 are withdrawn in view of the amendments made to the claims.

Claim Rejections - 35 USC § 112 1st paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following rejection has been previously presented

Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following factors have been considered in formulating this rejection (*In re Wands,* 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Nature of the Invention

The invention is drawn to a method of diagnosing cancer or a precancerous condition in a mammal. The method comprises (a) obtaining a cell or tissue sample from a mammal suspected of having cancer or a precancerous condition and determining for said sample the gene copy number of the HSPC150 gene (b) comparing said gene copy number of step (a) to the gene copy number of the HSPC150 gene from a sample of a corresponding cell or tissue from a mammal of the same species not having cancer of the type being diagnosed whereby a higher gene copy number determined in step (a) relative to that in step (b) indicates the presence of a cancer or pre-cancerous condition in the mammal of step (a) and results in a diagnosis of cancer or a pre-cancerous condition in said mammal. Thus the nature of the invention requires a reliable association between an increased copy number of the HSPC150 gene and

the presence of cancer or a precancerous condition. The invention is in a class of inventions which the CAFC has characterized as 'the unpredictable arts such as chemistry and biology" (Mycolgen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Federal Circuit 2001)).

Scope of the Claims:

The claims encompass a method wherein the cancer or precancerous condition is any type of cancer (breast, colon, cervical, lung, brain etc) or any type of precancerous condition (actinic keratosis, atrophic gastritis, cervical dysplasia etc). Only claim 7 is limited to specific cancers wherein the cancer is selected from the group consisting of breast, colon, lung, prostate, ovarian, pancreatic, cervical, and kidney cancer. Additionally the claims encompass a method for diagnosing cancer or a precancerous condition in any type of mammal (human, cat, whale, bat). Only claim 6 is limited to a specific type of mammal wherein the mammal is a human. Further the claims encompass obtaining a cell or tissue sample wherein the cell or tissue is derived from anywhere (i.e., saliva, hair, breast tissue).

Teachings in the Specification and Examples:

The specification teaches that the present invention relates to genes that have been identified as being amplified and/or over expressed, which can include increased copy number thereof, in cancerous cells. The genes have been identified through a combination of CGH, SKY, expression analysis, and reverse transcriptase PCR. The genes are listed in Table 1.

In the instant case the elected gene, HSPC150 protein similar to ubiquitin-conjugating enzyme, is listed in Table 1. Specifically Table provides the following information about HSPC150-- serial no: 119, SEQ ID NO: 107, Accession no: AI990409, tissue: breast, p_m: metastatic, chromosome: 1, band: q32.1, unigene: Hs.5199.

The information present in Table 1 is problematic for several reasons. First of all Table 1 does not indicate if the HSPC150 gene is over expressed, if it has an increased copy number, or both. Here it is important to note that increased expression is not necessarily equivalent to increased copy number. The specification (page 27) even states that if a gene is found to be present in multiple copies it may not be actively being over expressed. Therefore based on the limited information provided in Table 1 the specification does not provide support for the HSPC150 gene having an increased copy number in cancer or pre cancerous conditions. Additionally it is noted that Table 1 teaches that the tissue is breast. Here its unknown if this means that the HSPC150 gene was only associated with breast cancer (opposed to the other types of cancers and pre cancerous conditions encompassed by the claims) or if this means that the HSPC150 gene was only detected is breast tissue samples (opposed to being detected in other types of samples encompassed by the claims). Further its unclear if the genes that were identified as being amplified and/or over expressed, were detected in a representative number of different types of mammals since the claims encompass any mammal.

State of the Art and the Unpredictability of the Art:

As discussed above the specification does not provide support for the HSPC150

gene having an increased copy number in cancer or precancerous conditions since Table 1 does not indicate if the HSPC150 gene was over expressed, if it had an increased copy number, or both. Stranger (Science 2007 Vol 315 pages 848-853) supports the argument that increased expression is not necessarily equivalent to increased copy number. Stranger teaches that evidence has been presented that increased copy number can be positively or negatively correlated with gene expression levels. For example deletion of a transcriptional repressor could serve to elevate gene expression (see page 849, col 1). For this reason a finding that the HSPC150 is over expressed in cancer or pre cancerous conditions would not necessarily mean that the HSPC150 has an increased copy number in cancer or precancerous conditions. If possible applicants should clarify if the HSPC150 gene actually had an increased copy number, if it was over expressed, or both.

Additionally even if the HSPC150 gene was found to have an increased copy number in breast cancer it is highly unpredictable as to whether the results obtained could be extrapolated to other cancers and pre cancerous conditions. For example Adnane (Oncogene 1991 Vol 6 pages 659-663) teaches that the analysis of 387 human breast tumor DNAs revealed that BEK (also called FGFR2) was amplified in about 12% of the cases (page 659, col 2). On the other hand Sasaki (Brain Tumor Pathology 2003 Vol 20 pages 59-63) teaches a genome microarray spotted with 287 target genes was used to analyze resected tissue from 11 different high grade gliomas. A high frequency of deleted genes was observed in 6 of 11 cases (54.5%), including FGFR2 (abstract). These papers are relevant to the present situation because they support the argument

that it is highly unpredictable as to whether the amplification of HSPC150 in breast cancer could be extrapolated to other cancers and precancerous conditions.

Further even if the HSPC150 gene was found to have an increased copy number in humans with breast cancer it is highly unpredictable as to whether the results obtained could be extrapolated to other mammals. Knowledge that a particular gene such as HSPC150 is amplified in one organism (i.e. humans) with breast cancer does not allow one to conclude that this gene will also be amplified in other organisms with breast cancer.

Quantity of Experimentation:

In the instant case there is no evidence in the specification that increased copy number of HSPC150 is actually associated with cancer or precancerous conditions. For this reason one would have to conduct extensive experimentation. For example, such experimentation may involve using probes specific for HSPC150 gene to detect the copy number of the HSPC150 gene in large number of samples obtained from all different types of mammals with all different types of cancer and precancerous conditions. Such random, trial by error experimentation is considered to be undue. The specification has provided only an invitation to experiment.

Conclusions:

Taking into consideration the factors outlined above, including the nature of the invention and breadth of the claims, the state of the art, the level of skill in the art and its high level of unpredictability, the guidance provided by the applicant and the specific

examples, it is the conclusion that an undue amount of experimentation would be required to make and use the invention.

Response To Arguments

4. In the response filed February 16, 2010, the Applicants traversed the enablement rejection.

Applicants respectfully disagree and assert that they have made the art predictable by providing the sequence to be measured and the phenotype (i.e., increased copy number) to be determined. They state that Applicants' filing of the application is a constructive reduction to practice and Applicants teach all that is necessary to carry out the claimed method. The argue that Applicants teach that the subject gene (HSCP150) is related to breast cancer (see page 28, line 17, of the application as-filed, where breast cancer is linked to the first 229 genes). Further, Table 1, at gene No. 119 (SEQ ID NO: 107) clearly teaches that this gene is related to breast cancer metastasis (columns 4 and 5 of the table). Applicants state that while that is true that the claims are drawn to the use of any mammal and any type of cancer, the steps of the assay are clearly recited and are limited to measuring copy number of a stated gene. The identity of the mammal to be diagnosed and/or the cancer to be detected is not relevant to practicing the claimed method and is in no way limiting. The nature of a diagnosis is "to find out" and thus knowing the mammal and/or the tissue to be tested is not essential to the claimed method. If it were, one would know the answer to the question before they perform the diagnostic method of the claims. Regarding Table 1 the Applicants state that Table 1 is a list of genes identified in cancerous cells as being

both over-expressed and showing increased copy number. The Applicants have further submitted a paper by Lemaire which teaches that HSPC150 is over expressed in human head and neck tumors. The Applicants further state that other mammals are often successfully used as models for cancer in humans and that Applicants' claimed method provides a means of making just such a determination. Furthermore, Applicants assert that no undue experimentation is necessary.

These arguments have been fully considered but are not persuasive. The specification (page 6) states that the present invention relates to a set of genes that are amplified and/or over expressed genes in cancer cell lines and have been localized to various chromosomal regions of interest. In the instant case it is not clear from Table 1 if the HSPC150 gene is over expressed, if it has an increased copy number, or both. Based on the limited information provided in Table 1 the specification does not provide support for the HSPC150 gene having an increased copy number in cancer or pre cancerous conditions. Additionally it is noted that Table 1 teaches that the tissue is breast. Here its unknown if this means that the HSPC150 gene was only associated with breast cancer (opposed to the other types of cancers and pre cancerous conditions encompassed by the claims) or if this means that the HSPC150 gene was only detected is breast tissue samples (opposed to being detected in other types of samples encompassed by the claims). Even if the specification did teach a reliable and robust correlation between increased copy number of HSPC150 and breast cancer it would be highly unpredictable if there would also be a reliable and robust correlation between increased copy number of HSPC150 and the other types of cancers that are

encompassed by the claims. The specification does not provide any evidence that other cancers will also have an increased copy number of HSPC150. The paper by Lemair which teaches that HSPC150 is over expressed in human head and neck tumors is not really relevant because it is drawn to gene expression not copy number analysis. As discussed in the rejection increased expression is not necessarily equivalent to increased copy number. Further since the claims encompass any mammals it is relevant to point out that the Applicants have not provided any evidence that the HSPC150 gene has an increased copy number in a representative number of different mammals. Since these issues have not been clarified the Examiner maintains the position that undue experimentation would be required to make and/or use the claimed invention. For example, such experimentation may involve using probes specific for HSPC150 gene to detect the copy number of the HSPC150 gene in large number of samples obtained from all different types of mammals with all different types of cancer and precancerous conditions. Such random, trial by error experimentation is considered to be undue. The specification has provided only an invitation to experiment. Case law has established that '(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that '(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the

art as well as the predictability in the art. Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that '(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement".

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 7:30 TO 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached at 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amanda M. Shaw
Examiner
Art Unit 1634

/Stephen Kapushoc/
Primary Examiner, Art Unit 1634